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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,769	01/04/2001	Roberto A. Macina	DEX-0109	8320

26259 7590 04/01/2004

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EXAMINER	
HARRIS, ALANA M	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 04/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,769	MACINA ET AL.	
	Examiner	Art Unit	
	Alana M. Harris, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 21 December 2003.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/04/01; 9/10/02; 12/01/2003.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-6, SEQ ID NO: 3) in the Paper received 21 December 2003 is acknowledged. The traversal is on the ground(s) that the "MPEP 803.04 clearly states that a reasonable number of nucleotide sequences... can be claimed in a single application". Applicants also aver the instant claims encompass four sequences and consequently does not place an undue burden on the Examiner and a restriction should not be required. The Examiner has reviewed the cited section of the MPEP, as well as the arguments. These points of view have been carefully considered but found unpersuasive. Applicants have not set forth any evidence disclosing SEQ ID NO: 3, 4, 5 or 7 are polynucleotide sequences from the same parent sequence or share a common core structure, see attached database sheets. Absent any evidence to the contrary each sequence is regarded as a separate invention due to the fact that each separate nucleic acid sequence encodes different products, which are materially different from one another. Moreover, any methods reciting these patentably distinct sequences are regarded as separate and distinct inventions.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-6 are pending.

Claims 1-6 are examined on the merits to the extent they read on SEQ ID NO: 3, a polynucleotide.

Claim Objections

3. Claim 6 is objected to because of the following informality: it contains reference to non-elected inventions. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth a CSG as mRNA, SEQ ID NO: 3 also known as clone ID 1341701 and gene ID 29634 (Cln106) and not variants, analogs or derivatives of SEQ ID NO: 3, which are to be implemented in Applicants' methods.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116). Applicant is

reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

Applicants are not required to disclose every species encompassed by a genus. For example as indicated in *The Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412),, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

Applicants broadly claim methods of diagnosing the presence, metastases of breast cancer in a patient, as well as staging and monitoring a change in stage of colon cancer in a patient evaluating the levels of CSG. However, Applicant is not entitled, nor is the specification enabled for the use of all variants, analogs and derivatives encompassed by the broad term, CSG. The CSG to be implemented in the examined claimed invention is the CSG identified as mRNA, SEQ ID NO: 3, which may or may not be effective as a colon cancer marker. Applicant is not permitted to claim all polynucleotides that are encompassed by the claims, hence not entitled to the wide breadth of the claims at issue. No disclosure of any other (examined) CSG, SEQ ID NO: 3-derived polynucleotides, beyond the mention of SEQ ID NO: 3 is made in the specification. The recitation "CSG" in Applicant's claims encompasses CSG variants. There is no description of what sites within the polynucleotide sequence of SEQ ID NO:

3 at which variability may be tolerated and no information regarding the relation of the encoded protein's structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure.

This is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. The recitation "CSG" in claims 1-6 is indefinite. Applicants are advised to amend claim 1 to include the full terminology before the first citing of the acronym. Hence, line 3 of claim 1 should be amended to cite, "...of colon specific gene (CSG) in a sample...".

b. The recitation "levels of CSG" is vague and indefinite in claims 1-5. It is not clear if the CSG to be measured is a polynucleotide, polypeptide or mRNA. Accordingly, the metes and bounds cannot be determined.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-5 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Number 5,733,748 (Document AA on IDS filed February 28, 2002). U.S. Patent #5,733,748 discloses methods for diagnosing the presence of colon cancer and metastases of colon cancer in a patient (see Abstract; column 1, paragraph 1; bridging paragraph of columns 7 and 8). These methods are based on determining the levels of colon specific genes (CSG) in samples from a patient's cells, blood and saliva (see column 8, lines 30-32; column 9, lines 17-20), determining levels of a CSG comprising a polynucleotide sequence and comparing the levels of CSG between colon cancer samples and non-diseased samples, see column 8, lines 10-16. It is the detection of active transcription, enhanced transcription or enhanced protein expression of a CSG in cells other than those derived from colon that is indicative of colon cancer metastases (column 8, lines 1-19). It is the Examiner's position that based on the disclosed methodology that it would be reasonable to conclude that clearly a patient with colon cancer had been identified. One of ordinary skill in the art would expect that the detection of metastasis would be determined at a period after diagnosis in order to evaluate growth of the cancer.

The specification on page 8, lines 7-19 defines staging in effect as analyzation of a patient's sample for CSG, comparison between said sample and a normal control for an increase and decrease in levels of CSG. Monitoring colon cancer is defined utilizing the parameters set forth in staging in addition to periodic assessment of the cancer's growth (see "Monitoring" section of starting on page 8-page 9). Interpreted in light of the specification it is clear the disclosed method of the prior art which sets forth differentiating cancer and metastasis would read on Applicants' claims of staging, monitoring changes (i.e. regression and remission) and progression of the diagnosed colon cancer.

10. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/39419 (Document AA on IDS submitted January 4, 2001). WO 96/39419 discloses methods for diagnosing the presence of colon cancer and metastases of colon cancer in a patient (see Abstract; page 1, paragraph 1; page 14, paragraph 1). These methods are based on determining the levels of CSG in samples from a patient's cells, blood and saliva (see page 14, last paragraph; page 15, first paragraph; page 34, second paragraph), determining levels of a CSG comprising a polynucleotide sequence and comparing the determined levels of CSG between colon cancer samples and non-diseased samples, wherein if the transcription or protein expression is enhanced it is indicative of colon cancer metastases and inherently indicative of the presence of the said cancer (see page 14, paragraph 2). It is the detection of active transcription, enhanced transcription or enhanced protein expression of a CSG in cells other than

those derived from colon that is indicative of colon cancer metastases. It is the Examiner's position that based on the disclosed methodology that it would be reasonable to conclude that clearly a patient with colon cancer had been identified. One of ordinary skill in the art would expect that the detection of metastasis would be determined at a period after diagnosis in order to evaluate growth of the cancer.

The specification on page 8, lines 7-19 defines staging in effect as analyzation of a patient's sample for CSG, comparison between said sample and a normal control for an increase and decrease in levels of CSG. Monitoring colon cancer is defined utilizing the parameters set forth in staging in addition to periodic assessment of the cancer's growth (see "Monitoring" section of page 8-page 9, line 13). Interpreted in light of the specification it is clear the disclosed method of the prior art which sets forth differentiating cancer and metastasis would read on Applicants' claims of staging, monitoring changes (i.e. regression and remission) and progression of the diagnosed colon cancer.

Double Patenting

11. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

12. Claims 1-5 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 2-6 of copending Application No. 10/276,115 (filed May 29, 2001). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

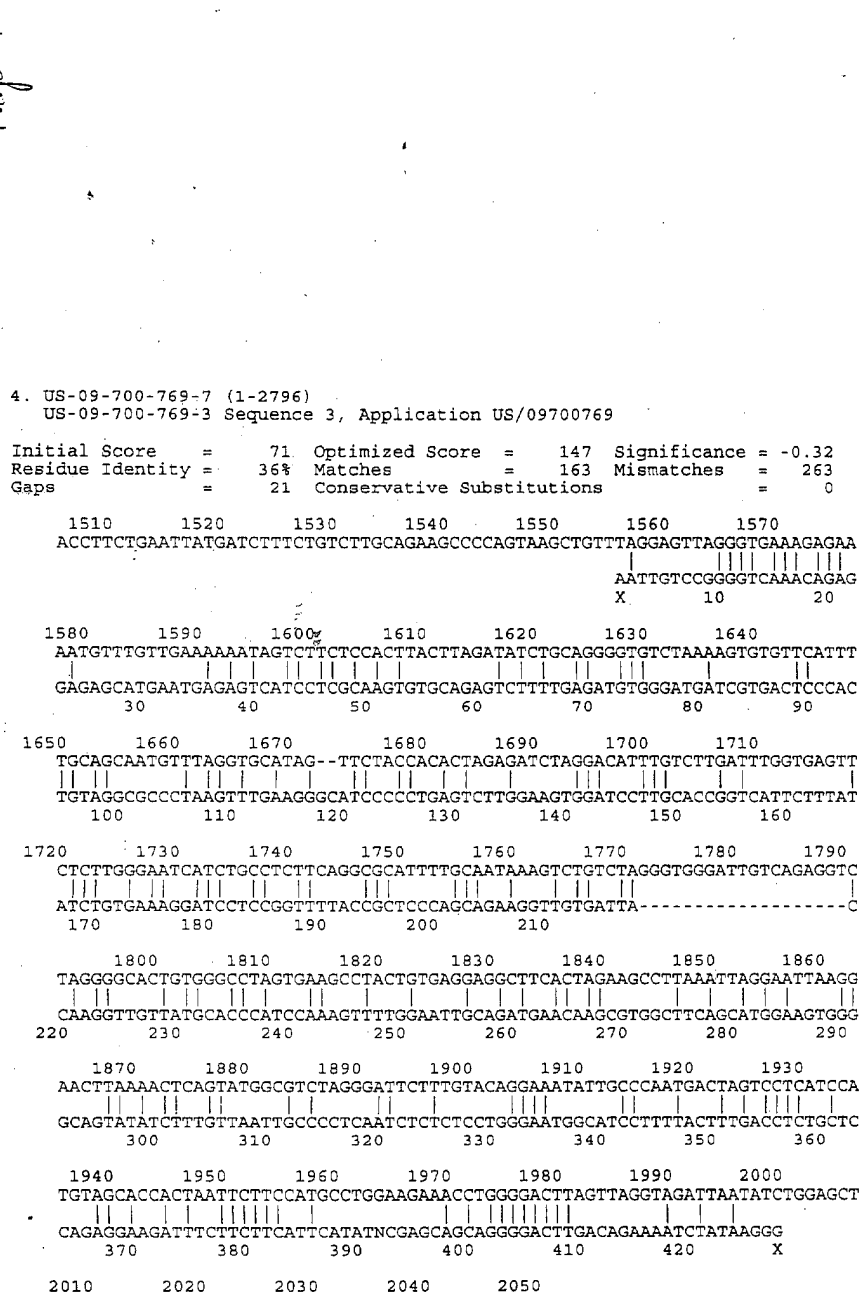
Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09/618,596 (filed July 17, 2000). Although the conflicting claims are not identical, they are not patentably distinct from each other because claim 1 of application '596 sets forth a method of detecting a CSG identified as SEQ ID NO: 1 and claim 1 of the instant application reads on a broad method of diagnosing a CSG. With the diagnosis of the broadly termed CSG encompassing a plethora of molecules, intrinsically the broad claim of the instant application reads on the detection of any CSG molecule.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. US-09-700-769-7 (1-2796)
US-09-700-769-3 Sequence 3, Application US/09700769

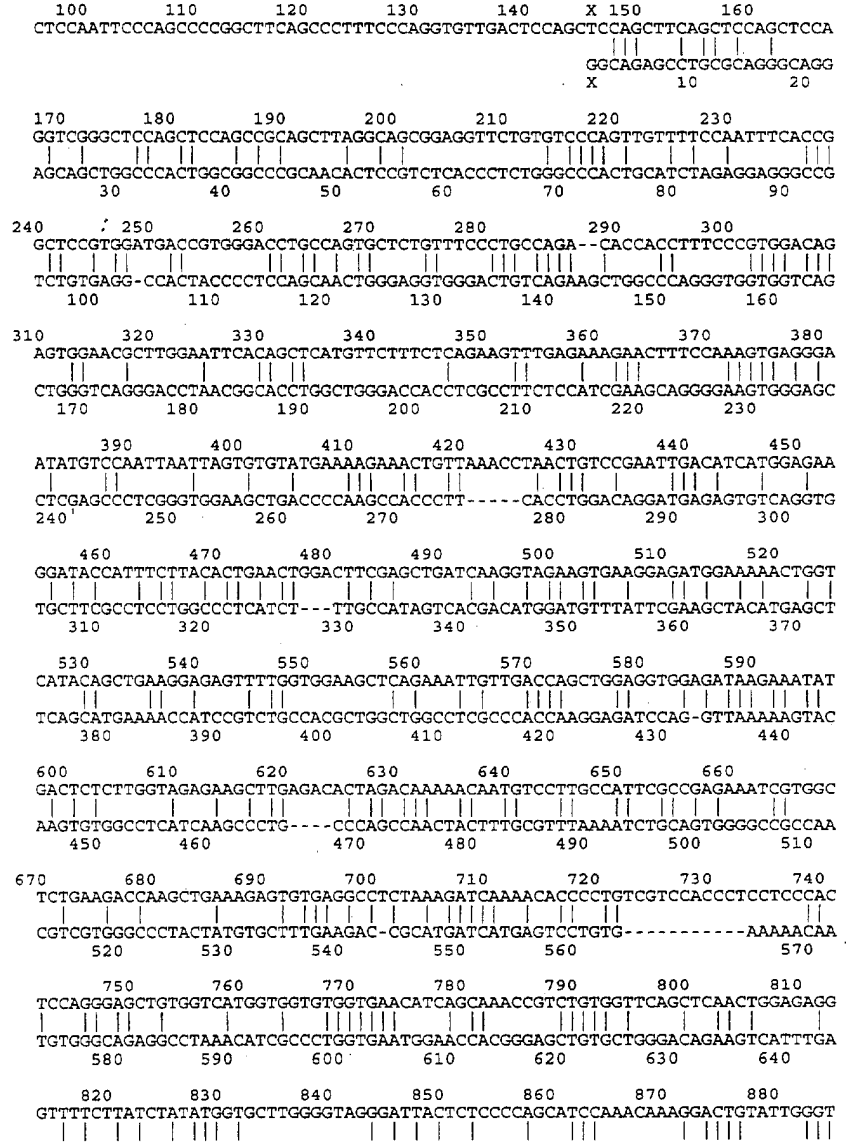
Initial Score = 71 Optimized Score = 147 Significance = -0.32
Residue Identity = 36% Matches = 163 Mismatches = 263
Gaps = 21 Conservative Substitutions = 0



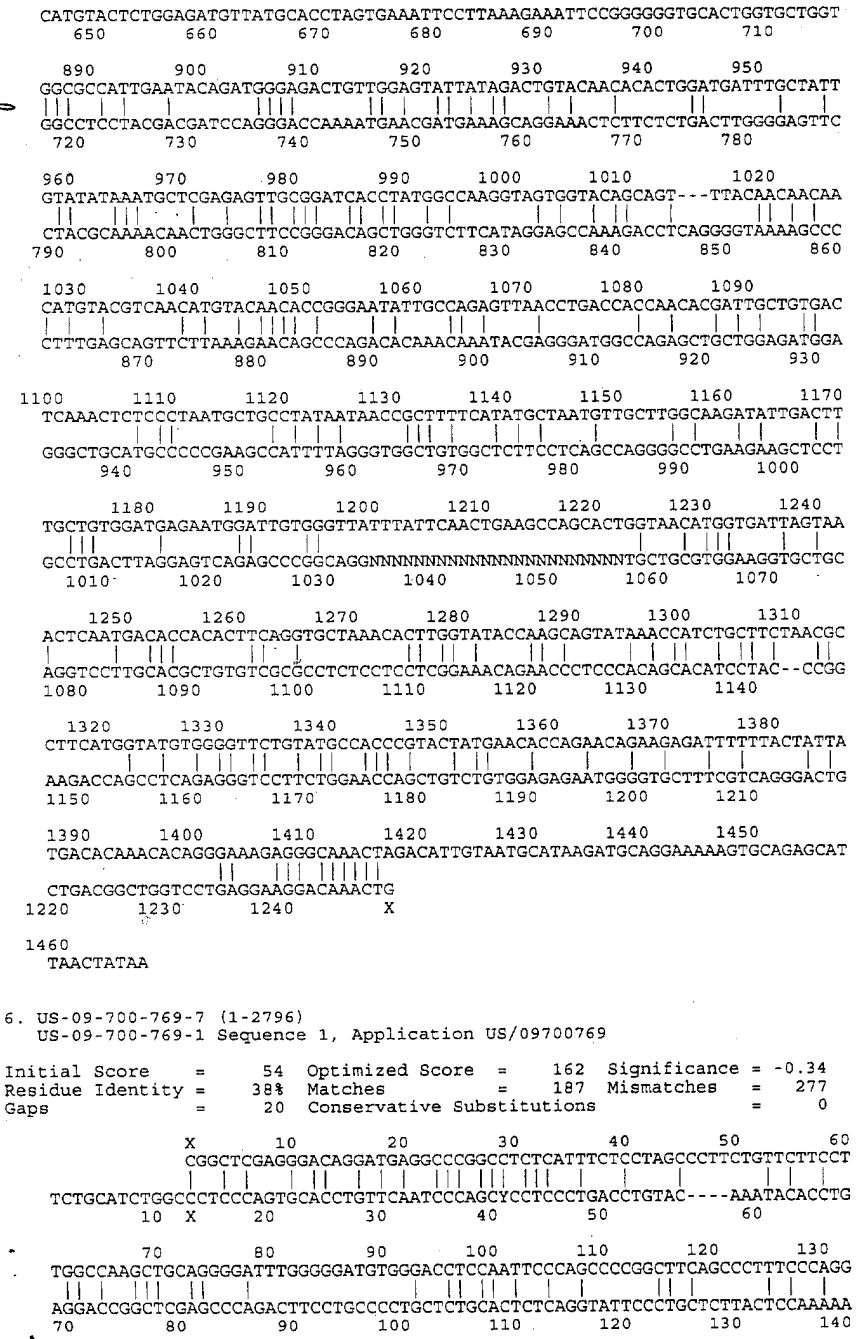
CCTCGAGGGACCAAATCTCCAACTTTTTTTTCCCCTCACTACA

5. US-09-700-769-7 (1-2796)
US-09-700-769-5 Sequence 5, Application US/09700769

Initial Score = 63 Optimized Score = 394 Significance = -0.33
Residue Identity = 35% Matches = 450 Mismatches = 794
Gaps = 33 Conservative Substitutions = 0

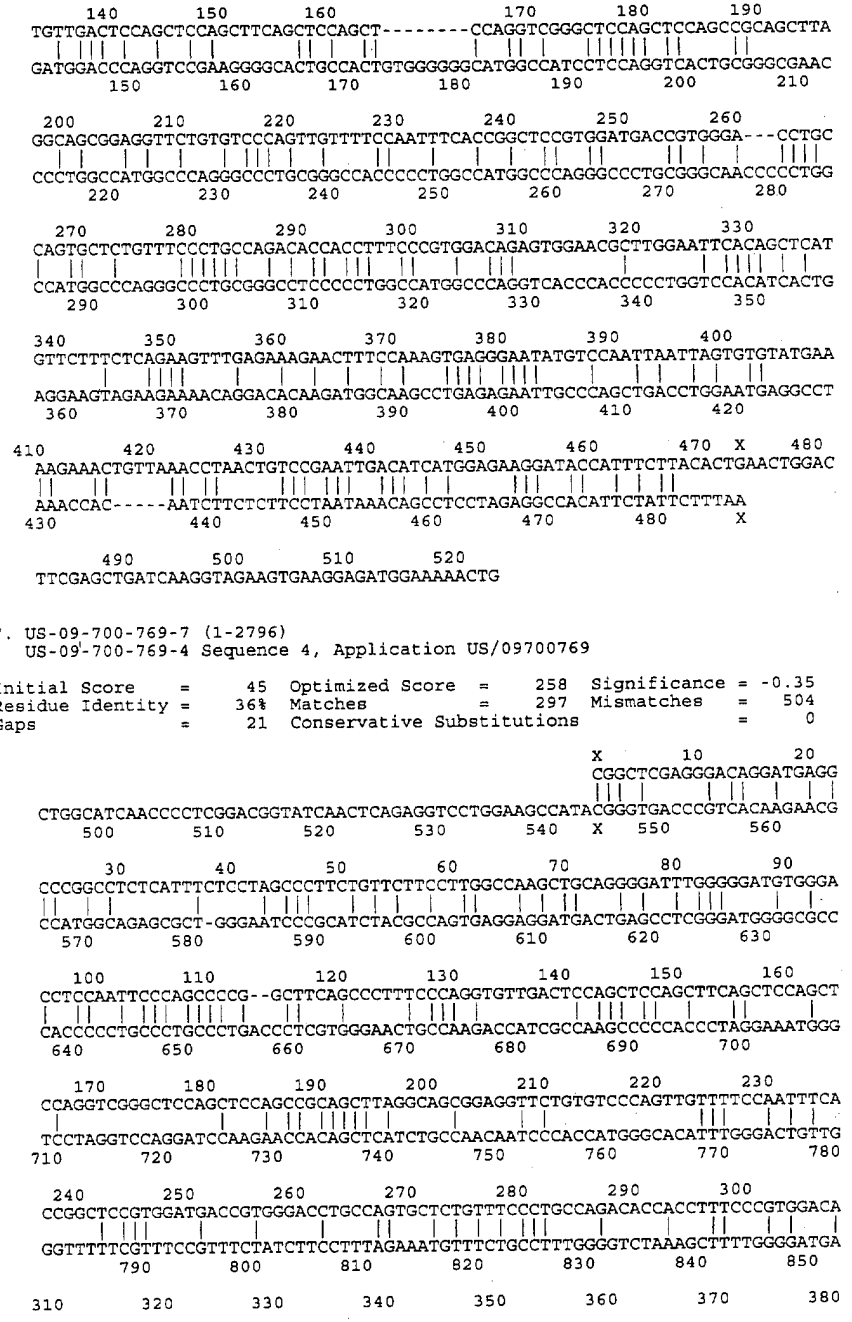


Page 11



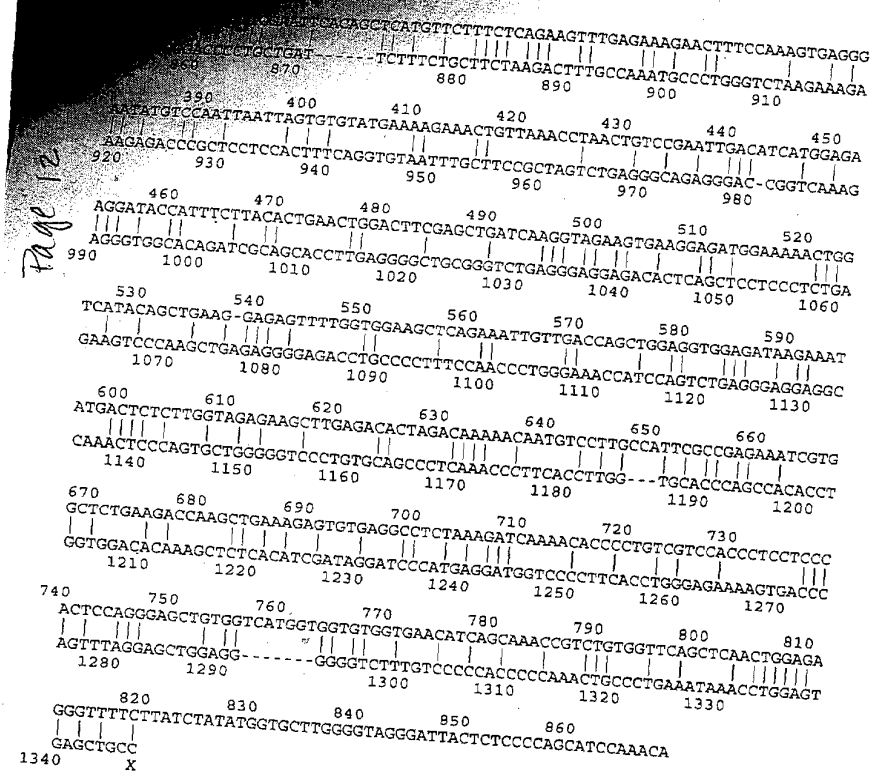
6. US-09-700-769-7 (1-2796)
US-09-700-769-1 Sequence 1, Application US/09700769

Initial Score	=	54	Optimized Score	=	162	Significance	= -0.34
Residue Identity	=	38%	Matches	=	187	Mismatches	= 277
Gaps	=	20	Conservative Substitutions				= 0



7. US-09-700-769-7 (1-2796)
US-09-700-769-4 Sequence 4, Application US/09700769

Initial Score	=	45	Optimized Score	=	258	Significance	= -0.35
Residue Identity	=	36%	Matches	=	297	Mismatches	= 504
Gaps	=	21	Conservative Substitutions				= 0



Conclusion

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is (571) 272-0831. The examiner can normally be reached between the hours of 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne "Bonnie" Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ALANA M. HARRIS, PH.D.
PRIMARY EXAMINER

Alana M. Harris, Ph.D.
26 February 2004